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RESEARCH PAPER

Relationships between Ambient Air Pollution, Meteorological Parameters and Respiratory Mortality in Mashhad, Iran: a Time Series Analysis

Mitra Mohammadi [1*], Morteza Hatami [2, 3], Reza Esmaeli [4], Samaneh Gohari [5], Mandana Mohammadi [6], Elahe Khayyami [7]

[1] Department of Environmental Science, Faculty of Environmental Science, Kheradgarayn Motahar Institute of Higher Education, P.O.Box, 9177934955,Mashhad, Iran
[2] Environmental Health Engineer, North Khorasan University of Medical Sciences, Iran
[3] Natural Resources Engineering-Environmental Pollution, Department of Environmental Science, Faculty of Environmental Science, Kheradgarayn Motahar Institute of Higher Education, Mashhad, Iran
[4] Urban Services of Mashhad Municipality, Environmental Pollutants Monitoring Center, Mashhad, Iran
[5] Environmental Health Engineering, Faculty of Health, Mashhad University of Medical Sciences, Mashhad, Iran
[6] Department of Statistics, Ferdowsi University of Mashhad, Mashhad, Iran
[7] Department of Environmental Science and Engineering, Islamic Azad University, West Tehran Branch, Tehran, Iran

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Abstract
The time series model has been exploited to estimate the relationship between meteorological variables and air in Mashhad with respiratory mortality. For this purpose, data on respiratory mortality was based on data recorded on March 2014 to 2015. In order to investigate the effect of meteorological variables and air pollution values on respiratory mortality, the Box- Jenkins time series model has been utilized. Moreover, the effect of age and seasons on the number of respiratory deaths was assessed by the linear regression and ANOVA test. The fit of the final model to determining the monthly relationship between meteorological variables and air pollutants with the number of respiratory mortalities is a (1,0,2) ARIMA. In the monthly survey, temperature and rainfall have the inverse relationship and pressure has the direct relationship with the average of 7.4, 3.2, and 17.42 on the respiratory mortality. It was also found direct relationship between the mortality from respiratory diseases and CO and O_3 and inverse relationship with SO_2, NO_2 and $PM_{2.5}$ pollutants with an average of 67.40, 17.42, 17.89, 6.83, and 0.68, respectively. Also, the results of this study indicate that older people are more likely to be affected by the inappropriate status of air quality by 0.37%. The results showed a significant difference between respiratory mortality in different seasons of the year, and the highest number of deaths occurred in the winter.

Keywords: Air Pollutants, Meteorological Variables, Respiratory Disease, Mortality, and Time Series Model

INTRODUCTION

In the last 50 years, air pollution and its effect on human health and the environment have interested globally. Detrimental health impacts of air pollution consist of a wide range of acute

* Corresponding author Email: mitramohammadi@gmail.com

and chronic health impacts. These harmful effects increase patient admissions, emergency visits and, as the most important part, increase the number of deaths. (Çapraz et al. 2016; Fang et al. 2016). Different studies demonstrate that all kinds of air pollution can impact the respiratory airways. Releases of gases such as carbon monoxide (CO), carbon dioxide (CO_2), nitrogen dioxide (NO_2), particulate matter (PM), sulfur dioxide (SO_2), and ozone (O_3) have an intense effect on public health like coughing, wheezing, and asthma and increasing respiratory and cardiovascular diseases (Agudelo-Castañeda et al. 2019). Moreover, microorganisms in air pollutants cause infectious diseases such as tuberculosis, influenza, and other viral infections. The high concentrations of sulfur dioxide (SO_2) and nitrogen dioxide (NO_2) created symptoms like nose and throat irritation and bronchoconstriction (López-Villarrubia et al., 2010; Çapraz et al., 2016; Fang et al., 2016; Zhu et al., 2017). According to World Health Organization reports, 1.3, 3.7, and 4.2 million deaths in 2008, 2012, and 2016 happened because of air (Çapraz et al., 2016; Mokoena et al., 2019; Dastoorpoor et al., 2020). It was also found that 29% cancer, 17% acute lower respiratory tract infection, 24% brain stroke, 25% ischemic heart disease, and 43% chronic obstructive pulmonary disease of total deaths related to air pollution (Dastoorpoor et al., 2020). Air pollution immediately affects the respiratory system. Afterward, its effect has been created as an influence and worsen factor on various respiratory diseases such as lung cancer, bronchitis, chronic obstructive pulmonary diseases, pneumonia, asthma, and influenza. The top three leading causes of non-communicable disease mortality are respiratory diseases, and accordingly, it is essential to notice risk items and convenient preventive measures (Mokoena et al., 2019).

Numerous studies have been conducted in recent years in different parts of the world as well as in Iran to determine the relationship between the effects of air pollution and meteorological variables on human health (Wong et al., 2010). Based on Zhou et al., 2015 air pollution had a positive and statistically significant impact on the elderly respiratory mortality rate in China. The most considerable effect happened in northern cities during cold months. According to Khamutian et al ., 2015 a significant relationship between CO, O_3, NO_2, and temperature with emergency room visits because of asthma in Kermanshah was observed, and there is no relationship between SO_2 and particulate matter. This study displayed CO as an air pollutants effects on asthma, and the temperature has a role in intensifying asthma. Dadbakhsh et al. 2017. also found an inverse relationship between mean temperature due to mortality and respiratory death in all individuals and women. This study showed cold temperatures can increase the number of deaths due to respiration; therefore, policies to reduce mortality in cold weather should be implemented. Taneepanichskul et al., 2018 also found an association between PM10 exposure and daily mortality.

Mashhad is one of the metropolises of Iran due to the existence of historical and cultural monuments especially the Holy shrine of Imam Reza. The existence of pleasant climates and also numerous universities is one of the most attractive cities for pilgrimage, tourism and immigration. The current tourism system of Mashhad, while having positive effects on the economy (like employment, income, etc.), and socio-cultural field; has faced the city with instabilities in various sectors of ecology, socio-cultural and economic, the most important of which can be referred to the issue of air pollution. Pollutants such as SO_2, NO_2, and $PM_{2.5}$ have a significant relationship with cardiovascular mortality in Mashhad. In addition, the relationship between meteorological variables and air pollution with the number of cardiovascular mortality is observed (Hatami et al. 2017; Manochehrneya et al. 2020). Therefore, there is a need to conduct studies related to the relationship between meteorological variables and air pollution with mortality from respiratory diseases in Mashhad in recent years.

Due to the increase in air pollution crisis in recent decades and the decline in the number of healthy days, especially in metropolitan areas, as well as the growing trend of disease, mortality and its damage, taking serious measures to reduce air pollution is one of the most important needs of our society, which can be achieved through better knowledge and wider study. Therefore, the purpose of this study is to evaluate the relationship between meteorological variables, air pollutants and respiratory disease mortality in Mashhad by time series model in 2014.

MATERIALS AND METHODS

The city of Mashhad, the capital of Khorasan Razavi province with an area of 328 square kilometers in northeastern Iran and at a longitude of 59 degrees and 15 minutes to 60 degrees and 36 minutes and latitude of 35 degrees and 43 minutes to 37 degrees and 8 minutes and in the catchment area of Kashfarud, is located between the Binalood Mountains and Hezar Masjid. The height of the city from the sea level is about 1050 meters (maximum 1150 meters and minimum 950 meters). The city of Mashhad has had a high population growth in the last century so the population of this city in 2016 was 3,001,184 people and is considered the second-largest city in Iran after Tehran. Also, the share of Moving resources in the total emission of the five main pollutants is about 64%. The share of personal vehicles in gaseous pollutants is 38% and its particles are 7/2%. The industrial situation of Mashhad is important due to the existence of different mineral resources and the concentration of production centers and food, textile, electricity, electronics, chemical, pharmaceutical, cellulose and other metallic and non-metallic industries. Figure. 1 shows the geographical location of Mashhad in Iran.

This study used three different data sets, including the concentration of air pollutants, meteorological data, and information related to respiratory mortality. Problems and limitations such as access to data, data collection, standardization of statistical period, and the quantity and quality of available statistics caused the statistical period of 2014, which had the complete data, to be selected for this study.

A total of 11765 data, including the average 24-hour concentration of each air pollutant (CO, NO_2, SO_2, O_3, and $PM_{2.5}$) was collected from 11 air quality measuring stations in different parts of Mashhad, which is registered in the Environmental Pollution Monitoring Center of Mashhad for the duration of 2014/3/21 to 2015/3/20 (365 days, 52 weeks and 12 months) (Table1). Then, the concentration of air pollutants was arranged based on average, minimum, and maximum on daily, weekly, monthly and seasonal scales.

Data related to meteorological variables including temperature, pressure, relative humidity,

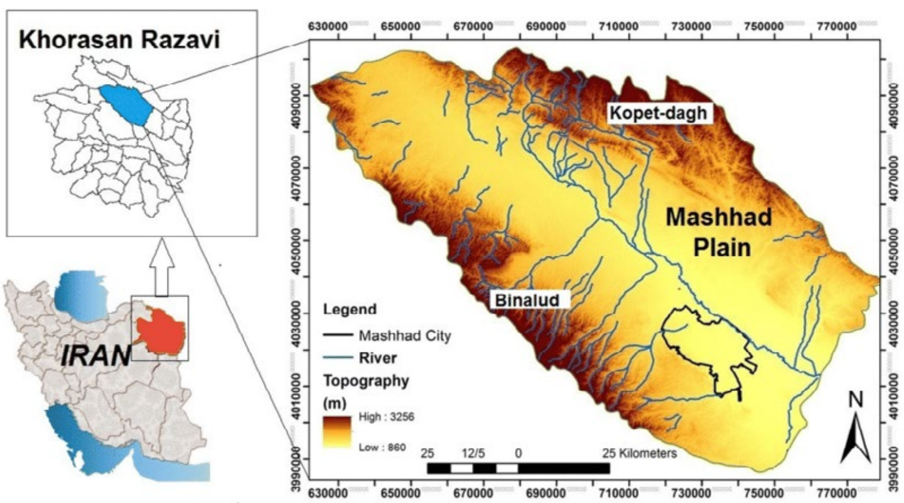

Fig. 1. Geographical location of Mashhad, Iran

Table 1. Location of Mashhad Air quality measuring stations

NO.	Name of Station	Station Type	(X)	(Y)
1	Toroq	Suburbs Urban (Upstream)	737146	4011577
2	Taghiabad	Traffic	732384	4019364
3	Sadaf	Traffic	723820	4023433
4	Vahdat	Traffic	736075	4018900
5	Sajad	Urban (residential)	728498	4022777
6	Nakhresi	Urban (residential)	734682	4016991
7	Sakhteman	Suburbs Urban	741027	4016880
8	Resalat	Urban (residential)	737210	4022276
9	lashkar	Urban (residential)	723788	4027366
10	Vila	Urban (residential)	723118	4022361
11	Khayam	Urban (mobile)	729921	4021975

wind speed, and rainfall were also collected during the study period from the Meteorological Organization of Mashhad and were arranged in daily, weekly, and monthly time scales. Considering that the pressure data were measured at 3-hour intervals, the data were calculated based on the daily average. Then, the climatic factors were arranged based on average, minimum and maximum on daily, weekly, monthly, and seasonal scales.

Data related to respiratory mortality were collected on daily, monthly, and yearly time scales in 2014 from the Ferdows Organization of Mashhad. This statistic includes 1875 cases of respiratory mortality (such as Pneumonia, Acute bronchitis, Chronic bronchitis, Asthma, Respiratory disorders, Intrapulmonary diseases, and other lung diseases). Mortality data included additional information such as age, date of birth (day, month, and year), place of death, and the deceased's place of residence which were used in statistical analysis.

This research is a cross-sectional descriptive-analytical study using time series regression. Firstly, the research's theoretical topics and experimental studies were collected by reviewing the literature, and then, the appropriate analytical model was selected. A time series is a set of observations about a variable measured at discrete points in time, usually at equal distances, and arranged in time. Thus, a time series from observing a phenomenon over time is obtained. Among the advantages of the time series model is its need for less extra information, which has led to a greater tendency to use it. Therefore, the time series model was used in this study to describe the information according to the data which has been collected and sorted over time and at equal intervals.

The collected data's daily, weekly, monthly, and seasonal values were calculated, and SPSS (20) and R (3.3.0) software were used for statistical analysis. Firstly, the outliers' package and the seasonal autoregressive integrated moving average (SARIMA) model were used in R (3.3.0) software to identify outliers and missing data. Although the effect of changes in meteorological variables and air pollution on the human body can be seen on the same day, climate change has consequences in many cases that may affect other days. For this purpose, the influence of health effects from meteorological variables and air pollution at different time intervals was investigated by applying time delays in this study. Hence, the Box-Jenkins time series model (Autoregressive Integrated Moving Average) was used to investigate the effect of meteorological variables and air pollution on respiratory mortality with a lag of daily, weekly, and monthly time scales at a significant level of 5% ($P < 0.05$). Then, the effect of age and seasons on the number of resulting death was investigated by linear regression and ANOVA test, respectively. It should be noted that in this statistical method, meteorological variables and also air pollutants are independent variables, and on the other hand, meteorological variables and time (day, week,

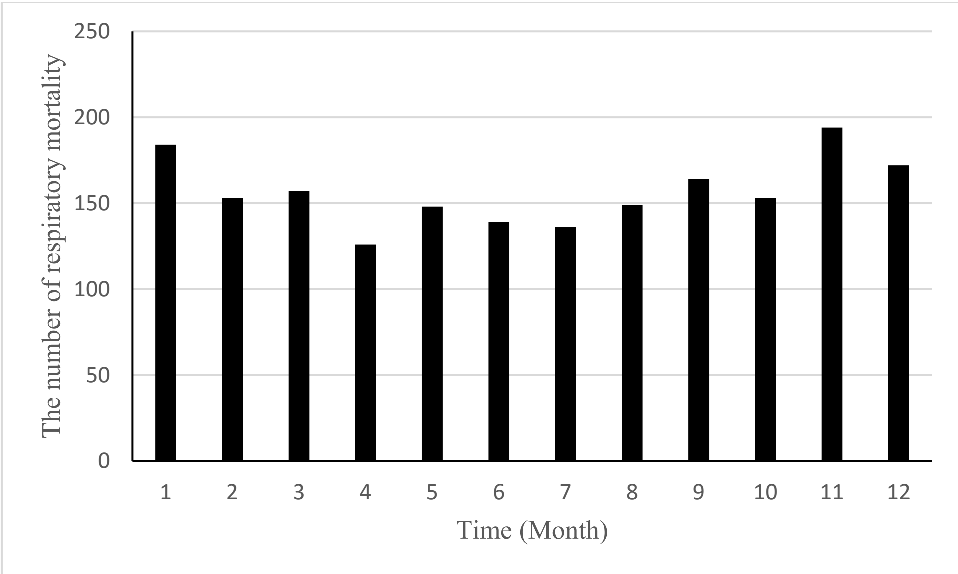

Fig. 2. Monthly average of respiratory mortality in Mashhad in 2014

month, and season) are confounding factors in the model and the respiratory mortality are as the dependent variable in the study.

RESULTS AND DISCUSSIONS

The average mortality caused by respiratory diseases in Mashhad in 12 months of 2014 was 156 persons. The lowest and highest rate of mortality was 126, 194 persons and its standard deviation was 19.6. Figure. 2 indicates the number of respiratory mortalities in different months of 2014. The highest and the lowest number of respiratory mortalities was in January and then in March (378 persons) and June (126 persons), respectively (Figure. 2). The high mortality rate in the cold months can be caused by the frequency of the weekend phenomenon these days. In a thermal inversion, the air stabilizes, and particles accumulate within the inversion layer, increasing the severity of air pollution. It means cold and heavy air is at the bottom, and hot and light air is at the top. It causes the polluted air to remain in the vicinity of the ground. In the inversion layer, the temperature is higher than the lower layer, thus preventing colder air from rising, and eventually, the polluted material condenses beneath it. These conditions usually occur on clear nights without winter clouds. In other words, the intensity of inversions was higher in the cold period of the year than in the warm period. Conversely, in hot weather, heat is transferred to the surrounding air, and as a result, air movement performs well, and air pollution decreases (Apostol et al., 2015).

The monthly average of meteorological variables including pressure, humidity, temperature, wind speed, and rainfall was 903.3 hPa, 49.1 %, 16.04 °C, 6.83 m/s, and 23.66 mm, and the concentration of $PM_{2.5}$, NO_2, O_3, CO, and SO_2 in monthly scale was 27.6 μg/m3, 22.21 ppb, 14.87 ppb, 1.81 ppm, and 13.63 ppb, respectively. The maximum pressure and humidity were in November, and the maximum temperature and wind speed were in June. The minimum pressure, humidity, temperature, and wind speed were in June, July, November, and November. The highest rainfall was in March, and its lowest amount was in June, July, and August. Also, the highest concentrations of $PM_{2.5}$, NO_2, O_3, CO, and SO_2 were in August, February, May, March, and May, respectively. The lowest concentrations of these pollutants were in February, January, November, August, and July, respectively. The increase in the concentration of suspended particles in August

Table 2. Iran Clean Air Standards Approved in 2016

Maximum allowed to repeat in one year	ppm	μg/m³	Type of pollutant
No indicators have been announced	Carbon Monoxide (CO)		
	9	10000	Maximum 8 hours
	35	40000	Maximum 1 hours
	Sulfur Dioxide (SO_2)		
	0/075	196	Maximum 1 hours
	0/14	395	Maximum 24 hours
	Nitrogen Dioxide (NO_2)		
	0/053	100	Annually
	0/1	200	Maximum 1 hours
	PM_{10}		
	-	-	Annually
	-	150	Maximum 24 hours
	$PM_{2.5}$		
	-	12	Annually
	-	35	Maximum 24 hours
	Ozone(O_3)		
	0/075	159	Maximum 8 hours
	-	-	Maximum 1 hours
	Lead		
	-	0/5	Annually
	-	0/15	Moving quarterly average
	Benzene		
	-	5	Annually

can be attributed to the lack of rainfall and drought on the ground and soil, the loss of vegetation at the end of the dry and hot period of the year, which enters Mashhad in the form of dust or dust storms from the suburbs and neighboring areas. The higher concentration of NO_2 and CO in February and March should be considered with the increase in traffic in Mashhad in these two months, because February is the last month of the solar year and urban travel increases, and March coincides with the Nowruz holiday, which is a large number of pilgrims and Tourists flock to Mashhad. In this regard, the increase in O_3, which is a secondary pollutant, can be attributed to the availability of conditions for the formation of this pollutant in the atmosphere of Mashhad. Where NO_x and sunshine are abundantly available, which of course is in the first place in the study year, May, with a slight difference from the other warm months of the year.

Finally, the increase in SO_2 this month could also be due to increased traffic, or this requires more accurate statistical assessments.

In addition, it should be noted that the concentration of all mentioned pollutants is below the standard threshold of the Health Act in 2016 (Table 2). It was also found that the amount of pollutants is much higher on a single day than its monthly average. For example, on some days, the concentration of NO_2 and SO_2 was 0.06 ppm and 0.05 ppm, respectively, and the $PM_{2.5}$ concentration was 105.1μg/m³.

Investigation of the monthly relationship between meteorological variables or parameters and Air pollutants with respiratory mortality

Fitting the final model to determine the monthly relationship between meteorological

Table 3. Parameters of the final model determination of the relationship between monthly mortality due to respiratory disease with meteorological variables and air pollutants

Variable's name					Meteorological Variables				Air Pollutants			
	Intercept[c]	Coefficient			Pressure (hPa)	Temperature (°c)	Rainfall (mm)	$PM_{2.5}$ (µg/m ^{3})	NO_2 (ppm)	O_3 (ppm)	CO (ppm)	SO_2 (ppm)
		ar1[a]	ma1[b]	ma2[b]								
Estimatied Coefficient	-15339	-0.9826	-1.7427	0.9367	17.4286	-7.4099	-3.2094	-0.6876	-6.8338	17.4299	67.4067	-17.8979
Standard Error	587.4567	0.0213	0.4386	0.2853	0.6565	0.1527	0.1073	0.0366	0.2036	0.5145	2.604	0.5346
p-value[d]	<0.0001	<0.0001	0.001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

a=ar1 is autoregressive component of the first stage

b= ma1 and ma2 are second-order moving average model components

c= Intercept is width from source

d= The significance level of the model (the probability value that measures the degree of compatibility of the sample data with the result of null hypothesis (H_0)).

variables and air pollutants with the number of respiratory mortalities was performed using a purely random model of ARIMA (1, 0, 2). The coefficients of meteorological variables and air pollutants in the final model and the extent of their relationship with the outcome (number of respiratory mortality) are shown in Table 3. The final equation for computing this model is as follow,

(1) $Yt = -15339 - 0.9826_{yt-1} - 1.7427_{et-1} + 0.9367_{et-2} + 17.4286$ Pressure $- 7.4099$ Temperature $- 3.2094$ Rainfall $- 0.6876\ PM_{2.5} - 6.8338\ NO_2 + 17.4299\ O_3 + 67.4067\ CO - 17.8979\ SO_2 + et$

Yt represents dependent variable (respiratory mortality) and et, error of time series regression model at time t.

Based on Table 3, the ARIMA model showed that among the climatic elements, temperature (inverse relationship), rainfall (inverse relationship), and pressure (direct relationship) in the monthly survey, have had a significant relationship with the number of respiratory mortalities ($P<0.05$). Because the pressure variable has the most significant effect in terms of absolute value among these elements, it was found that the number of respiratory mortalities will also rise as the pressure increases. In fact, among the mentioned elements, the average pressure with superiority of 17.42 plays an essential role in increasing the number of death relative to temperature and rainfall. In comparison, the effect of temperature and rainfall was 7.4 and 3.2 units, respectively, in reducing the mortality rate (Table 3). Atmospheric pressure controls the circulation patterns of air masses, therefore changes in atmospheric pressure can alter temperature, rainfall, and winds, leading to the great health impact of climate change (Qu et al., 2014). Rainfall and temperature also have a negative effect, and their increase will raise respiratory mortality (Table 3). Rainfall is one of the most effective atmospheric factors in cleaning the air of pollutants. Polluted gases in the air were dissolved in rainwater, absorbed by the liquid, washed away, and then the suspended particles in the air were returned to the ground. The number of pollutants removed by precipitation, especially rain, depends on the intensity of rainfall, air pollution, and the size of raindrops (Mokoena et al., 2019). According to this study, temperature after pressure had the greatest effect on mortality due to respiratory diseases compared to other meteorological variables in Mashhad in 2014. The temperature variable is inversely related to respiratory mortality in our estimated model. In fact, low temperatures have been related with a large number of biological conditions considered risk factors for respiratory diseases from cross-infection, increased indoor crowding and also detrimental effect on the immune system's resistance to respiratory infection (Antunes et al., 2017). Additionally, Jacobson et al., 2021. reported that extreme temperatures may increase the risk of hospitalizations and deaths due to respiratory diseases, not only because of exposure to heat but also due to exposure to cold temperatures. Lin et al., 2011 assessed exposure to extremes of temperature and its effects on mortality among the elderly in Taiwanese cities. Consistence with our results, the risks of death from respiratory diseases were higher for low average daily temperatures when compared to high temperatures. In China, a study in Beijing estimated the effects of two-day cumulative exposure (by moving average) to average daily temperatures in the periods of heat (April to September) and cold (October to March) on mortality from respiratory diseases in the elderly aged 65 and over Liu et al., 2011. In the heat period, the risk of death was 8% (95% CI: 1% to 15%) for each 5 °C increase in the two-day temperature average, and in the cold period, the increase was 13% (95% CI: 6% to 20%). Probably, the physiological resilience of individuals should influence these results, as well as past illnesses. On the other hand, the results of this study showed all pollutants have a significant effect on mortality from respiratory diseases on a monthly scale ($p<0.05$). So O_3 and CO have a significant and positive relationship, and $PM_{2.5}$, NO_2, and SO_2 have a negative association with the rate of mortality due to respiratory diseases. The most destructive effect is related to the CO pollutant, with a coefficient of 67.40; as the concentration of this pollutant in the air increases, the rate of respiratory mortality will also rise (Table3). One of the most important air pollutants in big cities, including Mashhad, is CO, which is mainly due to the uncontrolled and rapid expansion of urbanization, industrialization, population growth, lack of proper transportation system and urban traffic, and lack of modern technology about cars and shortage of green space (Zhu et al., 2017; Mokoena et al., 2019). Song et al., 2019 found a significant relationship between exposure to CO, $PM_{2.5}$, PM_{10}, and hospital admissions because of high blood pressure; and in the cold seasons due to increased air pollutants. CO enters the bloodstream through the lungs and combines with hemoglobin in the blood. The affinity of this pollutant for blood hemoglobin is about 220 times higher than oxygen. The combination of CO with hemoglobin (oxyhemoglobin) reduces the amount of oxygen that reaches the tissues and organs of the body and, in high concentrations, causes changes in heart function and respiration and lastly coma and death (Dastoorpoor et al., 2020). Shortness of breath and burning of the airways are also important symptoms of CO poisoning. O_3 also causes symptoms such as coughing, shortness of breath, constriction of the airways, respiratory disorders, and changes in red blood cells (Maji et al., 2017; Tajudin et al., 2019). However, the scientific aspects of O_3's adverse effects are still under question. Issues such as its acute or chronic effects, confounders, or its interaction with climate variables and other pollutants are still not well understood. Nevertheless, its adverse effects are important because nowadays the levels of O_3 are much higher than in the preindustrial times (Dastoorpoor et al., 2018). Guo et al .,2014 indicate that O_3 has a substantial health burden on mortality in Thailand. According to their pooled national estimate from the single pollutant model, a 10 ppb increase in daily O3 was associated with an increase of 0.78% (95% PI: 0.20, 1.35%) in non-accidental mortality. In addition, in this study, SO_2 showed inverse relations with respiratory mortality that was likely caused by its transformation to sulfuric acid (H_2SO_4) (Lu et al., 2019). The inverse relationship between NO_2 and the outcome is related to the high reactivity of this pollutant leading to the formation of other pollutants such as O_3. Therefore, NO_2 is negatively correlated with respiratory mortality and its effect on health outcomes should be analyzed as a combined effect of O_3 and NO_2 (known as the Ox effect) (Abed Al Ahad et al., 2020). The existence of an inverse relationship between some pollutants and the rate of mortality due to respiratory diseases in the fit of the current model can be due to the simultaneous consideration of the role of meteorological variables and air pollutants on mortality, the effect of other confounding factors such as smoking, sex, level of education, car ownership, improper diet, inactivity, type of job, social and economic stress, duration of contact with the environment, etc., more susceptibility of these pollutants to cofounding factors including meteorological variables and their high self-relationship (Agudelo-Castañeda et al., 2019; Dehghani et al., 2017). Capraz et al (2016) found a positive association between PM_{10}, SO_2 and NO_2 with respiratory mortality in Istanbul. Moreover, in five cities in South Brazil, an increase of 10 $\mu g/m^3$ in the monthly average concentration of PM_{10} was associated with an increase in respiratory hospitalizations in all age groups, with the maximum effect on the population aged between 16 and 59 years (IRR: Incidence rate ratio 2.04 (95% CI: Confidence interval = 1.97-2.12)). For NO_2 and SO_2, stronger intermediate-term effects were found in children between 6 and 15 years, while for O_3 higher effects were found in children less than 1 year (Agudelo-Castañeda et al., 2019).

On the other hand, the present study showed that the mentioned pollutants and meteorological variables have long-term effects (monthly) and not immediate or short-term (daily and weekly) on human health. An investigation of the daily relationship between meteorological variables and air pollutants with respiratory mortality which is known as the short-term or acute effect shows that among the climatic elements, only wind speed has a significant relationship with the rate of respiratory mortality ($p < 0.05$) in this study. While other climatic elements and all air pollutants do not have a significant relationship with mortality due to respiratory diseases on the same day (results not shown). This might be due to a small number of daily patients, the existence of many interfering factors (like smoking, type of job, season, social and economic stress, duration of exposure to the outside environment, etc.), and also the impossibility of

Table 4. Parameters of the model for determining the relationship between age with respiratory mortality in Mashhad in 2014

Variable	Estimatied Coefficient	Standard Error	t statistic*	p-value*
Intercept	-3.17	3.32	-0.95	0.341
Age	0.37	0.05	6.91	<0.0001

eliminating some other factors in this study. In some other studies like Shao et al., 2021, similar results also have been observed indicating the lack of daily association between climatic elements and the concentration of pollutants with acute respiratory attacks. Therefore, this issue should be considered in epidemiological studies of air pollution, and in similar studies, longer (annual) periods should be used.

A monthly survey of the number of respiratory mortalities based on different ages in 2014 in this study indicates that the average age of people was 53.5, the minimum age was one year, the maximum was 106 years, and the standard deviation was 3.6.

For statistical analysis of the relationship between age and respiratory mortality, a linear regression model (generalized model) was used. Generalized linear regression allows us to use methods similar to those for linear models in cases where the response variables have abnormal distributions and in cases where the relationship between the response variable and the explanatory variables is not linearly simple. A generalized linear regression will typically model the 'observed amount' (e.g. mortality rate) as:

Amount or frequency = Base level × Factor 1 × Factor 2 …,

while taking account automatically of the relationship in the data. The generalized linear regression output will consist of a 'base level' number and, for each factor, a series of multiplicative coefficients showing the relative effect of belonging to a particular level of that factor (Cerchiara, et al., 2008). In this model, age is the factor used as the independent variable (X), while the dependent variable (Y) is respiratory mortality. The relevant coefficients and the impact rate of their relationship with the outcome are shown in Table 4. The model results showed that age significantly impacts mortality due to respiratory diseases as its p-value is lesser than 0.05 (p-value<0.0001). Since the estimated coefficient of this variable is a positive value, it could be said that age directly affects the mortality rate of patients. If age increases by one unit (year), the rate of death due to respiratory diseases elevates by a coefficient of 0.37 (Table 4). Mortality in old age can be caused by factors such as a weakened immune system, excessive work activity outside the home, and the combination of other factors affecting respiratory disease such as smoking, and mental health problems. According to the results of Agudelo-Castañeda et al., 2019 the number of respiratory diseases in all age groups elevates when the mean concentrations of PM_{10}, SO_2, CO, NO_2, and O_3 increase about 20%. It was also reported that PM10 impacts younger groups and children below five years, while NO2 affects children between 6–15 years old.

*= In the linear regression model (generalized), the H0 is there is not any relationship between age with respiratory mortality and the H_1 is there is a relationship between age with respiratory mortality, and therefore the t-Statistic and p-value are measured the meaningful of these hypotheses.

Limited studies have been carried out on the relationship between air pollution and mortality in different seasons of the year (hot and cold). Since the amount of air pollution is different in several seasons of the year. Consequently, the rate of disease and mortality will be altered. Therefore, the present study has investigated the effect of seasons on mortality due to respiratory diseases. The number of mortalities based on different seasons in Mashhad in 2014 shows that the average mortality, standard deviation, minimum and maximum were 468.8, 23.5, 413, and

Table 5. Analysis of the Variance (ANOVA) test to investigate the effects of seasons on mortalities from respiratory disease

Source of Changes	Sam of Squares	df	Mean Square	F	P-value
Between Groups	92.808	3	30.936	4.438	0.004
Within Groups	2516.343	361	6.97		
Total	2609.151	364			

Table 6. Post hoc tests (LSD) to investigate the difference between mortality from respiratory disease in different seasons

Post hoc test	Season(I)	Season(J)	Mean Difference (I-J)	Standard Error	P-value	95% confidence interval	
						Lower Bound	Upper Bound
LSD	1	2.0	0.8710*	0.3872	0.025	0.11	1.632
		3.0	0.3229	0.3904	0.409	-0.445	1.091
		4.0	-0.5196	0.3915	0.185	-1.29	0.25
	2	1.0	-0.8710*	0.3872	0.025	-1.632	-0.11
		3.0	-0.548	0.3904	0.161	-1.316	0.22
		4.0	-1.3906*	0.3915	0	-2.161	-0.621
	3	1.0	-0.3229	0.3904	0.409	-1.091	0.445
		2.0	0.548	0.3904	0.161	-0.22	1.316
		4.0	-0.8426*	0.3947	0.033	-1.619	-0.066
	4	1.0	0.5196	0.3915	0.185	-0.25	0.29
		2.0	1.3906*	0.3915	0	0.621	2.161
		3.0	0.8426*	0.3947	0.033	0.066	1.619

Season 1= Spring, 2 = Summer, 3= Autumn and 4= Winter

*= I and J are not abbreviated; they are used only for a symbol as the number of groups. In this study, there are 4 groups (seasons), so that each group is compared with other groups in LSD post hoc test, respectively.

519 persons, respectively.

The effect of different seasons on mortalities from respiratory disease was evaluated by comparing the average of several independent groups using the Analysis of the Variance (ANOVA) test. ANOVA provides an analytical study for testing the differences between group means and it uses F-tests to statistically test the equality of means. F-statistics are based on the ratio of mean squares. Table 5 shows the sum of squares, the degrees of freedom, the mean of the squares, the t-test, and the p-value. The H_0 hypothesis in this test states that there is no significant difference between the seasons in respiratory mortality. Table 5 shows that the F-value is greater than the F-critical value for the alpha level selected (0.05). Therefore, we have evidence to reject the null hypothesis and say that at least one of the four seasons has significantly different means and thus belongs to an entirely different population. Moreover, since the p-value obtained in this part is less than 0.05 (p-value = 0.004), it can be stated that there is a significant difference between the mean respiratory mortality rate in different seasons of the year (Table 5).

According to the mentioned results and significant differences in different seasons, LSD post hoc test has been conducted to detect the difference between groups (Table 6). The results indicate a significant difference between the mortality rate of respiratory diseases in spring and summer

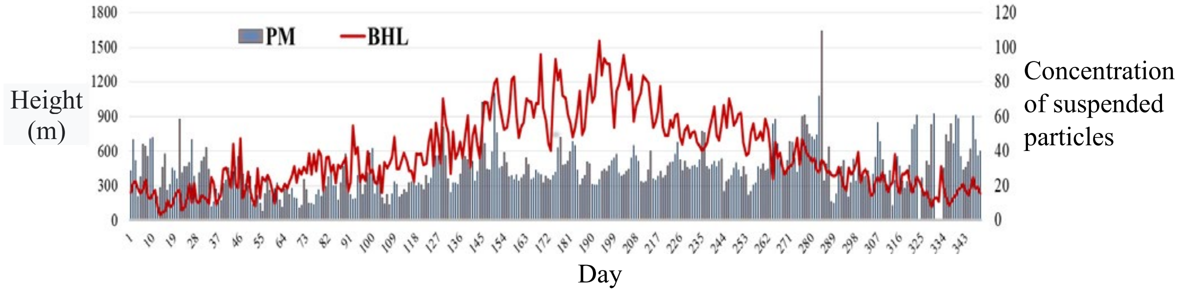

Fig. 3. Daily changes of pm2.5 concentration and height of temperature inversion layer (bhl) in Mashhad

at the level of 0.05%. This number was higher in spring than in summer. There is no significant difference between mortality in spring and autumn, and its number was slightly higher in spring than in autumn. However, most deaths due to respiratory diseases record in winter, and the number of deaths due to respiratory diseases in spring and winter is not significantly different ($p > 0.05$). There was a significant difference ($p < 0.05$) in mortality in summer, autumn, and winter so the number was higher in winter than in summer and autumn. Mortality rates in summer and autumn are not significantly different ($p > 0.05$), and the number of deaths in autumn was higher than in summer. In summary, this study showed that the highest mortality rate due to respiratory diseases occurred in winter, spring, autumn, and summer, respectively (Table 6). In the cold months, due to the decrease in the amount of sunlight, the increase in the cloudiness of the sky, the stability of the air, and finally, the inversion phenomenon; the accumulation of pollutants near the earth's surface increases, and this phenomenon can have a significant impact on increasing mortality from respiratory diseases (Zhu et al., 2017). On the other hand, the cold air and high-pressure flow on the city intensify during these months, which lead to a decrease in temperature. This is often due to the temperature gradients that have formed. The tabs of these temperature gradients decrease as they penetrate the city due to a reduction in thermal gradient and wind speed over the city. This cold air fall on the city can effectively intensify the temperature inversion that causes the accumulation of pollutants below its surface (Çapraz et al., 2016). Mashhad is prone to temperature inversion due to arid and semi-arid climate as well as proximity to Siberian high pressure so that over 300 days a year with temperature inversion (different types with different intensity and weakness). According to Figure. 3, the daily changes of suspended particles and the height of the boundary layer have been shown to decrease with the height of the layer with increasing pollutant concentration in the cold period of Mashhad.

According to the study by Mokoena et al. (Mokoena et al., 2019), daily ambient air pollutants had noticeable seasonal differences with the amount of $PM_{2.5}$ and SO_2 during the cold months. This seasonal trend confirms the continued reliance on coal combustion for energy sources, particularly during winter; furthermore, the increase of motor vehicles results courses elevated traffic emissions.

CONCLUSIONS

It can be concluded that time-series studies, which are the relation between the level of day-to-day air pollutants and health endpoint (mortality), consistently show a relationship between all causes of mortality. So, the aim of this study is to eliminate the effect of specific confounding factors (mainly meteorological variables and time-variable) and consider other characteristics of time series data to address the relationship between meteorological variables and air pollution with respiratory mortality. The results of the ARIMA model (1,0,2) indicate a significant relationship between the monthly mean of CO (direct relationship), O_3 (direct relationship), SO_2 (inverse relationship), NO_2 (inverse relationship), and $PM_{2.5}$ (inverse relationship) as well as meteorological variables such as pressure (direct relationship), temperature (inverse relationship) and rainfall (inverse relationship), with mortality from respiratory disease. Since the pressure and CO have the most important effect regarding their absolute value among these variables, it was found that with 1% increase in the abovementioned parameters, the rate of respiratory disease mortality will increase by 17.42% & 67.40% respectively. On the other hand, the study shows that these emissions with meteorological variables have a long-term impact (i.e., monthly here) and not immediate or short-term (i.e., daily and weekly) on human health. Therefore, this issue should be considered in epidemiological studies and other long periods studies (i. e. yearly) had better to be used. It was also found that the effects of air pollution are often seen in the elderly so the mortality rate due to respiratory diseases increases with age and if the age rises by one unit (year), the death rate due to the mentioned diseases elevate by a factor of 0.37. This study showed a significant difference between the mean of mortality due to respiratory diseases in different seasons and the highest rate of mortality from the mentioned diseases in the studied year occurred in winter, spring, fall, and summer, respectively. Due to the low concentration of pollutants and their significant relationship with some cases of mortality from respiratory diseases, it can be concluded that minor changes in pollutants' concentration can affect health and even the quality of human life and paying no or less attention to these pollutants can deprive the next generation of breathing in pure air, which is every human's right. Hence, besides recommending identifying different pollutant sources, it is needed to monitor the air pollution consistently and take the necessary actions to identify the causative factors and correct them. Moreover, it is recommended that advanced statistical methods such as the generalized linear model (Generalized Linear Model) and generalized additive method (Generalized Additive Model) are applied in order to accurately evaluate and eliminate overlap the effect of other factors in future studies. It is also important to examine the effect of other factors like smoking, gender, education, improper diet, inactivity, type of job, social and economic stress, or duration of contact with the outside environment in similar studies. Investigating the relationship between climatic elements and air pollutants with mortality due to respiratory disease is also suggested for longer periods of time (annually and more).

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CONFLICT OF INTEREST

The authors declare that there is not any conflict of interest regarding the publication of this manuscript. In addition, the ethical issues, including plagiarism, informed consent, misconduct, data fabrication and/ or falsification, double publication and/or submission, and redundancies have been completely observed by the authors.

LIFE SCIENCE REPORTING

No life science threat was practiced in this research.

ABBREVIATIONS

ARIMA= Autoregressive Integrated Moving Average
ANOVA= Analysis of Variance
CO= Carbon Monoxide
O_3= Ozone
SO_2= Sulfur Dioxide
NO_2= Nitrogen Dioxide
SPSS= Statistical Package for Social Science
LSD= Least Significant Difference

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